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The Mandarin Childhood Autism Spectrum Test (CAST): sex differences

Autism Spectrum Conditions (ASC) are neurodevelopmental disorders and are characterised by impairments in social interaction and communication, alongside the presence of unusually repetitive and stereotyped behaviours, and unusually narrow interests and activities (American Psychiatric Association, 2000). Prevalence estimates of ASC in the UK have increased greatly, from 4.8 per 10,000 in 1979 (Wing & Gould, 1979) to 116.1 per 10,000 in 2006 (Baird et al., 2006). The prevalence estimate was reported to be 113 per 10,000 in the US in 2012 (Centres of Disease Control and Prevention, 2012). The sex ratio in prevalence estimates for boys versus girls has been reported to be around 4:1 in general populations (Coleman, 1978; Fombonne, 2005; Lord & Schopler, 1985; Volkmar, Szatmari, & Sparrow, 1993; Wing, 1976) and higher in cognitively relatively higher-functioning children with ASC (Gillberg, Cederlund, Lamberg, & Zeijlon, 2006). Sex differences in the social and communication profiles related to ASC have been investigated for decades in the West (Lai et al., 2011; Lotter, 1966) but the underlying mechanism is not yet fully understood (Baron-Cohen, Knickmeyer, & Belmonte, 2005b; Baron-Cohen et al., 2011).

At a behavioural level, sex differences in children with an existing diagnosis of ASC have been explored. However, findings have been inconsistent. Unusual visual responses and inappropriate stereotyped play have been found to be more common in boys with ASC than in girls examined using the Psycho-educational Profile (PEP)

(Lord, Schopler, & Revicki, 1982). Sex effects have also been found in social play on the Autism Diagnostic Interview-Revised (ADI-R) (McLennan, Lord, & Schopler, 1993). Recent studies focusing on the association between sex and genetic susceptibility to ASC suggest that girls with ASC are less severely affected than boys in repetitive stereotyped behaviours dimension (Szatmari et al., 2012). However, another study using the ADI-R, not only reported no sex differences (Pilowsky, Yirmiya, Shulman, & Dover, 1998) but also found that girls had more autistic-like symptoms than boys, in terms of both social-communication and attention problems than boys (Holtmann, Bolte, & Poustka, 2007). Such findings may reflect referral patterns, which could be different for boys and girls.

In population samples, sex differences have been found in the amount of eye-contact made by infants at 12 months old (Knickmeyer, Baron-Cohen, Raggatt, & Taylor, 2005). Males and females have also been reported to have a different style of friendships (Baron-Cohen & Wheelwright, 2003), communication, and focus of attention (Baron-Cohen, 2003). Females may have better superficial social and communication skills (Gillberg & Coleman, 2000; Lai et al., 2011) and more appropriate play and interests than boys (Kopp & Gillberg, 1992; Wolff & McGuire, 1995). However, studies using participants matched according to age and IQ have reported inconsistent results (Lai et al., 2011). These inconsistent results may be partly due to variations in study methodology (Hartley & Sikora, 2009).

The Extreme Male Brain (EMB) theory has been proposed to explain the observed sex differences in behaviours (Baron-Cohen, 2002), and suggests that ASC may be an extreme of the typical male brain in the domains of empathy and systemizing (Baron-Cohen, Knickmeyer, & Belmonte, 2005a). Empathising is the drive to recognise another person's feelings, thoughts and intentions and respond to these with an appropriate emotion (Baron-Cohen & Wheelwright, 2004). Systemizing is the drive to identify variables of a system via an inductive process such as repeated observations to identify the underlying rules about how the system works (Baron-Cohen, 2002; Baron-Cohen, Richler, Bisarya, Gurunathan, & Wheelwright, 2003). According to the EMB theory, the male brain is more biased towards systemizing than empathising, while the female brain is more biased towards systemizing than empathising, while female brain is more biased towards empathising than systemizing (Baron-Cohen, 2002). At a general population level, instruments developed on the basis of the EMB theory, such as the Empathy Quotient (EQ) and the Systemizing Quotient (SQ), have also provided evidence for sex differences (Baron-Cohen, 2003; Baron-Cohen & Wheelwright, 2004).

In relation to screening instruments designed to identify autistic traits, previous depend on the description of possible autistic behaviours in daily life. Higher scores for boys than girls on screening instruments have also provided evidence of sex differences in children with ASC (Lai et al., 2011). Such differences have been founded in studies using the Autism Spectrum Screening Questionnaire (ASSQ) (Posserud, Lundervold, & Gillberg, 2006), the Social Responsiveness Scale (SRS)

(Constantino et al., 2003), the Autism Spectrum Quotient (AQ)(Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008; Baron-Cohen, Hoekstra, Knickmeyer, & Wheelwright, 2006) and the Childhood Autism Spectrum Test (CAST) (Williams et al., 2008). Autistic behaviours could be heterogeneous among different target populations, especially populations from other cultures. Previous research has suggested that a challenge is posed by the use of screening instruments developed in Western countries when used in Asian cultures (Wallis & Pinto-Martin, 2008). Possible differences in autistic traits between Western and Eastern cultures have been reported in terms of eye contact and early language development (Bernier, Mao, & Yen, 2010; Daley & Sigman, 2002). In Asian cultures, looking into another person's eye directly may be inappropriate, especially for people who have just met each other. However, avoidance of eye contact is an autistic trait that has been well recognised in Western studies. So far, limited research has been conducted to explore whether there are similar sex differences in autistic traits in Asian populations. One study has looked at empathising and systemizing in adults in Japan using the EQ and the SQ. Women on average scored significantly higher than men on the EQ, while men scored significantly higher than women on the SQ. This result provided some evidence that the sex differences in dimensions related to autistic traits are cross-culturally stable (Wakabayashi et al., 2007).

ASC is considered as a mental disorder. In China, due to the stigma towards psychiatric conditions, parents of children with ASC in China may not want to accept a diagnosis of ASC at first (McCabe, 2008; Sun et al., 2012). The recognition and

acceptance of this condition limits the awareness and knowledge of ASC in general population. In fact, certain cultural influence may have further delayed the identification of ASC. Interviews with parents of children with ASC in mainland China reported that many parents and grandparents consider that boys speak late is a good sign for future development (Sun et al., 2013). However, sex differences in autistic traits have not been directly investigated in the Chinese population in mainland China.

It has been suggested that many children with ASC, especially those with subtle manifestations, are not identified until primary school (Kamio, 2007). The CAST was developed as a screening instrument for ASC in primary school-aged children aged 4 to 11 years (Scott, Baron-Cohen, Bolton, & Brayne, 2002b), which was previously known as the Childhood Asperger Screening Test (Scott, Baron-Cohen, Bolton, & Brayne, 2002a; Scott et al., 2002b). This instrument can be used to detect children at risk for ASC more broadly and was therefore renamed as the 'Childhood Autism Spectrum Test'(Baron-Cohen et al., 2009).The CAST is a 37-item parent- completed questionnaire, of which 31 items contribute to the final score (Scott et al., 2002b). Within the 31 items, each item scores 1 for an ASC-positive response and 0 for an ASC-negative response. Thus, the CAST score ranges from 0 to 31 (Baron-Cohen et al., 2009). A score of 15 has been recommended as a cut-off point for the CAST (Scott et al., 2002b; Williams et al., 2005). CAST items measure social and communication skills in the following domains: the ability to initiate and maintain conversation and specific language difficulties, social interaction with peers and adults, play activities,

stereotyped and repetitive behaviours, choice of interests and sharing interests with others (Williams et al., 2008).

Sex differences have been investigated using the CAST in a Social Communication Research and Epidemiological (SCORE) study in UK primary schools (Baron-Cohen et al., 2009). In the SCORE study, the median score for boys (Median=5; IQR: 3, 8) was significantly higher than that for girls (Median=4; IQR: 2, 6) (*median test, p*<0.001). A much higher percentage of boys (n=81, 79.4%) was in the high score group (≥15), compared to girls (n=21, 20.6%)(Williams et al., 2008). The aim of the present study was to investigate using the same screening instrument, a Mandarin Chinese version of the CAST, whether similar sex differences exist in a Chinese population.

Method

Procedure

This study had full ethical approval from the Cambridge Psychological Ethics Committee and the Ethics Committee of the Peking University First Hospital (PUFH). A total of 737 children in school years 1-4 (6-11 years old) were recruited from two mainstream primary schools in Xicheng district of Beijing. The schools principals were approached and asked for participation. After the consent from the two principals, a screening package was sent to each child in school years 1-4 in the two

schools, which consisted of a screening questionnaire (the Mandarin CAST), an invitation letter and a consent form. The invitation letter informed the parents the purpose and procedures of this study, and invited the parents to participate. The screening packs were distributed by school-teacher to students for their parents to complete at home. After completion, the teachers collected the questionnaires from the students and returned them to the research team. After the consent was obtained from each participate, the questionnaires were used for analysis. The distribution and collection of questionnaires took one month.

Analysis

Missing responses to individual items were assigned a value of 0 (ASC-negative response) to generate a minimum score. If the questionnaire had more than 5 missing items, it was considered incomplete and was excluded from the analysis. Medians, inter-quartile ranges (IQR), standard deviation (SD) and ranges were used to describe these differences in item endorsements and distributions since the score distribution was skewed. The score distributions for boys and girls were compared using the Wilcoxon Rank Sum Test to test whether there was significant difference in the score distribution between boys and girls. The association between sex and score distribution across three score groups (≤11, 12-14, ≥15) was examined with a chi-squared Test. The differences in the proportions of ASC-positive scores for boys and girls on each item were tested using a chi-squared test. The effects of sex and age on

the continuous score were examined using linear regression. The association between possible variables and the CAST score groups was examined by logitsic regression. The unadjust odds ratios were provided for the effects of sex, age groups, father's education, mather's education, father's occupation, and mother's occupation. All the analyses were conducted in STATA 10.0.

Three sensitivity analyses were conducted to examine the effects of missing data:

1) Missing responses to individual items were assigned a value of 1 (ASC-positive response) to generate a maximum score. Analyses were repeated using maximum scores for both boys and girls.
2) Analyses were conducted using the minimum score for boys and maximum score for girls to estimate the most extreme effect of missing data on the observed sex differences.
3) The third sensitivity analysis excluded children who were given a diagnosis of ASC in the Mandarin CAST validation study.

Results

Data completion

In this study, n=737 questionnaires were distributed and n=714 (97%) were returned. Of the 714 CAST questionnaires, 655 (91.7%) were complete. 53 (7.4%) had one or

two missing items and six (0.8%) had three to seven items missing. 13 questionnaires were excluded due to missing information about sex and another 19 were excluded due to missing information about age or because the child was outside the age range (6-11). This left n=682 questionnaires for analysis. There were 360 boys and 322 girls. The mean age of the children was 8.4 years old (SD: 1.2). 627 (91.9%) Mandarin CAST questionnaires were fully completed. 54 (7.9%) questionnaires had missing values on 1 to 4 items.

Overall score distributions for boys and girls

The median score of the whole sample on the Mandarin CAST was 7.8 (IQR: 5, 10; range: 0, 21) (n=682). The median score for boys (median: 8.3; IQR: 6, 11; range: 0, 21) was higher than for girls (median: 7.2; IQR: 4, 9; range: 1, 21). The differences in the overall score distributions for boys and girls were significant (Wilcoxon Rank Sum Test*, $z=-4.329$, $p<0.001$*). Figure 1 provides the score distributions of boys and girls.

[insert Figure 1 about here]

Score distributions among three score groups

When the scores were categorised into three groups used in previous studies (Baron-Cohen et al., 2009)(low score: ≤11; borderline score: 12-14; high score: ≥15), the

differences in the proportions of boys and girls across all three score groups were significant (p=0.035) (see Table 1). Using logistic regression, only the association between sex and the CAST score groups was significant (Table 2). The unadjusted odds of being a boy increased 83% per score group (odds ratio=1.83, 95%CI: 1.14, 2.93, p=0.012). Using linear regression, no significant differences were found in mean scores between age groups (p=0.54). The distribution of scores in each age group is shown in Table 3.

[insert Tables 1, Table 2 and Table 3 here]

Item endorsement in boys and girls

The proportions of item endorsement by boys and girls are shown in Table 4. There were significant differences between boys and girls on seven items (items 8, 14, 21, 24, 29, 31 and 36). Within these seven items, the proportion of boys who scored as ASC-positives was significantly higher than that of girls.

[insert Table 4 here]

Sensitivity analyses

The analyses were repeated firstly using the maximum score. The mean maximum score of boys was 8.4 and that of girls was 7.3. The odds ratio for being a boy was the a little lower than before (1.77; 95% CI: 1.12, 2.82, *p*=0.015). When using maximum score for girls and minimum score for boys to estimate the extreme effect of sex, the odds ratio of being a boy was lower than those obtained previously (1.70; 95% CI: 1.07, 2.71, *p*=0.025). In these two sensitivity analyses, the same proportions of boys and girls were found in the high score group (boys: n=18 (60%), girls: n=12 (40%)).

After full diagnostic assessments, six children were given a diagnosis of ASC, all of whom did not have a diagnosis of ASC before. Four children were boys and two were girls. The mean score of remaining boys (8.2) was still higher than that of remaining girls (7.1). When these children were excluded, the effect of sex was similar to that obtained previously (odds ratio: 1.71; 95% CI: 1.08, 2.73, *p*=0.023). The number of boys in the high score group (n=16, 62%) was still greater than the number of girls (n=12, 38%).

Discussion

Overall findings

This study examined sex differences in relation to developmental profiles and autistic traits in a general population in mainland China. Boys on average had significantly higher scores on the Mandarin CAST than girls. This association was not influenced by age and was still observed when missing data were handled using different approaches. Autistic traits were found to be significantly higher in boys than in girls on seven Mandarin CAST items. This study provides evidence for sex differences in autistic traits in a Chinese culture.

Limitations

Several limitations should be noted. The sample was drawn from two ordinary schools in Beijing which are in close proximity to each other. Beijing may not be a representative of the whole population in mainland China due to its special political and economic status (National Bureau of Statistics of China, 2012). Thus, cautions need to be paid when applying results from this study to a national level. Previous studies have suggested possible differences in perspectives of children's behaviours between fathers and mothers (Donaldson, Elder, Self, & Christie, 2011; McCabe, 2008). However, it was not possible to measure observer influences due to the missing identity of informers of this study. In the future, this should also be taken into consideration. In addition, the cultural influence need to be taken into consideration when examine performance of the Mandarin CAST in Chinese population. Due to the possible different views in the development of boys and girls,

the endorsement of certain items in boys may be different from girls by Chinese parents in the first place. Thus, when interpreting the results, possible cultural effect should be kept in mind. In addition, more than 50% of the boys and girls scored as positive on items 6 (notice unusual details) and 19 (have an unusual memory for details). Over 40% of the boys and girls scored positive on item 14 (has an interest which takes up so much time). The general high endorsement of these items may be due to that the interpretation of these items by Chinese parents might be different from Western parents. Further investigation into the factor structure and a latent trait analysis of Mandarin CAST will be conducted and reported separately. There were missing values for certain items but sensitivity analyses showed that these were unlikely to influence the findings.

Behavioural differences between boys and girls

This study found that the differences in score distributions between boys and girls were consistent across age groups. This study also found that item endorsement was significantly different between boys and girls on seven items. Five items (items 8, 21, 24, 29 and 36) describe impairments in social interaction and communication, while two items (14 and 31) focus on narrow interests and repetitive behaviours. Item 29 ("Is his/her social behaviour very one-sided and always on his/her own terms?") and item 36 ("Does s/he often turn conversations to his/her favourite subject rather than following what the other person wants to talk about?") focus on the child's

communication difficulties. Item 21 (“Are people important to him/her?”) asks for the child’s perception of other people. Item 24 (“Does s/he play imaginatively with other children, and engage in role-play?”), item 31 (“Does s/he prefer imaginative activities such as play-acting or story-telling, rather than numbers or lists of facts?”) and item 8 (“When s/he was 3 years old, did s/he spend a lot of time pretending (e.g., play acting being a superhero, or holding teddy’s tea parties?)”) focus on the child’s social interaction (role-play) with peers. According to parents’ observations, boys’ behaviour in relation to these items was different from girls. Specifically, boys were reported to have more difficulties in social interactions, such as role-playing and taking turns, in communication. Boys were also found to have different approaches to friendship formation, confirming earlier studies (Baron-Cohen et al., 2003) and different types of play from girls, again confirming earlier studies (Knickmeyer et al., 2005). Also in agreement with previous findings, the current study provides further evidence that boys have narrower interests and more repetitive behaviours than girls. This has also been reported in two previous clinical studies based on diagnosed cases using face-to-face observation (ADOS) and parent interviews (ADI-R) (Lord et al., 1982; McLennan et al., 1993), whereas the current study used a parent self-completed screening questionnaire. Although different methods of sex comparisons have been used within and across cultures, there is consistency in these findings. Studies using comparable methods have reported higher proportions of autistic traits scores in boys. Typically developing boys have been found to score higher than girls in adult, child and adolescent versions of the AQ (Auyeung et al., 2008; Baron-Cohen et al., 2006; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). Boys aged 7-9 in a large population scored significantly higher on the ASSQ than girls

(Posserud et al., 2006). A study using the SRS to examine the autistic traits in 7-15 years old children reported that boys' scores were on average 25% higher than girls' (Constantino et al., 2003).

Implications and future directions

Sex differences in autistic features were found in a general population in mainland China. Although the Mandarin CAST was being applied in an Asian culture for the first time, the findings of this study suggested that differences in the developmental profiles between boys and girls may exist across cultures. Although the underlying reasons for these differences are still unknown, this finding has implications for further investigations into ASC in China and cross-culturally. First, it would be useful to conduct a population-based study that matches the IQs of boys and girls. Second, in order to rule out the effect of differences in study methodologies, further research could adopt a combination of direct observation, caregiver interviews and self-report questionnaires for data collection. Third, further developments in screening and diagnostic instruments need to take the different behaviours of boys and girls into account. Fourth, clinicians need to be aware of how ASC may differ in girls and boys when examining potential autistic cases. Girls may not show severe social and communication difficulties and they could have fewer inappropriate interests than boys. Fifth, the question of whether these differences can be traced at a genetic or biological level needs to be further investigated in order to improve our

understanding of the aetiology of ASC (Lai et al., 2011; Szatmari et al., 2012). Sixth, in terms of the implications of the Mandarin CAST, we should bear in mind the potential baseline sex differences. Since the score for boys was higher than that for girls, further studies need to examine whether it is reasonable to adopt a higher cut-off point for the Mandarin CAST for boys than for girls (Williams et al., 2008). Previous CAST studies have found significant sex differences in the general population but no differences between boys and girls with a diagnosis of ASC (Williams et al., 2008). It would be helpful to investigate whether sex differences exist among Chinese boys and girls with ASC using the Mandarin CAST.

Conclusions

This study shows that in the reports of autistic traits by parents of Chinese children, the same sex difficulties are seen that are found in Western populations. Sex differences may be universal across cultures and should be considered when developing screening and diagnostic instruments. Further research needs to be conducted to investigate the genetic, biological, neurological and other etiological mechanisms of these sex differences.

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